Insulin resistance, high prevalence of diabetes, and cardiovascular risk in immigrant Asians

SIR,—We read with interest the findings of Dhawan *et al*,[1] who highlighted the importance of hyperinsulinaemia, central obesity, and physical inactivity as risk factors in Asians with angiographically significant coronary artery disease. Both British and Indian Asians were found to share a predisposition to insulin resistance and its associated metabolic abnormalities—and hence a high cardiovascular risk. They conclude that this finding is likely to favour a genetic rather than environmental basis for the recognised high mortality in this ethnic group. However, migrants are not a random sample of the original population,[2] and their "selection" is likely to be determined by several health and socioeconomic factors, which are likely to influence their morbidity and mortality. If this environmental effect were a significant determinant of cardiovascular risk, one would not expect to see the high mortality from ischaemic heart disease (IHD) that has been recorded in Asians in South Africa,[3] Trinidad,[4] and Singapore,[5] who emigrated over a century ago.

We recently reported a survey in which we studied the cardiovascular risk factor profile of all Asian men admitted with acute myocardial infarction during 8 weeks to our city centre district general hospital in Birmingham, England, and to the San Fernando General Hospital, in Trinidad[6]: 74 patients were studied (55 patients (mean (SEM) age 58·1 (1·4)) in Trinidad (Trinidad group) and 19 in Birmingham (62·1 (2·6)) (UK Group) (table).

We also found that mean systolic and diastolic blood pressures were higher in those with hypertension in the Trinidad group (146·6 (16·9)/93·4 (11·4) mm Hg than in the UK group (120·8 (25·4)/75·0 (13·4) mm Hg, $P < 0·05$).[6] Though Asians in Trinidad have in many ways adapted to the lifestyle of the host population, this does not appear to have reduced their cardiovascular risk profile, because those admitted with acute myocardial infarction had, in fact, a greater prevalence of central obesity, smoking, and higher blood pressures than a similar group in England.[6]

Central obesity and physical inactivity were common to both communities in England and Trinidad and their relation to insulin resistance may be particularly important in Asians with IHD. Our data support the hypothesis of a genetic predisposition to central obesity and diabetes in Asians that seems to have been retained by third generation Asian immigrants in Trinidad. This may explain the persistently high mortality from IHD in Asians.

Risk factor profile of men admitted to hospital with acute myocardial infarction in Trinidad and Birmingham

	UK (%)	*Trinidad (%)*	*P value*
Prevalence of:			
Diabetes	32	36	NS
Hypertension	32	35	NS
Smokers	63	71	0·03
Regular alcohol use	42	91	<0·05
Regular exercise	21	11	<0·05
Mean waist to hip ratio (mean (SD))	0·95 (1·01)	1·01 (0·05)	<0·001

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1 Dhawan J, Bray CL, Warburton R, Ghambhir DS, Morris J. Insulin resistance, high prevalence of diabetes, and cardiovascular risk in immigrant Asians. Genetic or environmental effect? *Br Heart J* 1994;72:413–21.
2 Marmot MG, Adelstein AM, Bulusu L. Lessons from the study of immigrant mortality. *Lancet* 1984;i:1455–8.
3 Walker ARP. The epidemiology of ischaemic heart disease in the different ethnic populations in Johannesburg. *S Afr Med J* 1980; 57:784–82.
4 Miller GJ, Beckles GL, Maude GH, Carson DC, Alexis SD, Price SG, Byam NT. Ethnicity and other characteristics predictive of coronary heart disease in a developing community: principal results of the St James Survey, Trinidad. *Int J Epidemiol* 1989; 18:808–17.
5 Danaraj TJ, Acker MS, Danaraj W, Ong WH, Yam TB. Ethnic group differences in coronary heart disease in Singapore: an analysis of necropsy records. *Am Heart J* 1959; 58:516–26.
6 Farooqi IS, Dar S, Farooqi S, Beevers DG, Lip GYH. A comparative study of risk factors for acute myocardial infarction amongst men of Indo-origin in Trinidad and the UK. *Int J Cardiol* 1994;47:44–9.

Quality of life in heart failure treated with enoximone

SIR,—The Enoximone Investigators concluded that in severe heart failure enoximone reduces survival but has a beneficial effect on the quality of life of survivors.[1] As they indicate, if true, this is an important finding with interesting and difficult implications for drug regulatory bodies and for clinical practice. However, a statistical artefact could explain their results without there necessarily being any benefit from enoximone.

At randomisation, the two groups were reasonably well matched for measures of severity and other features. As the trial progressed there was differential mortality between the groups. It is not unreasonable to assume that those who died had more severe disease and a worse quality of life than those who survived. Thus even if there were no change at all in quality of life, the survivors will have a better average quality of life than the study group as a whole. Since more died in the enoximone group, this group will have lost more patients with poor quality of life, and enoximone will appear to have been beneficial.

Other evidence from the paper supports this interpretation of the results, namely, the greater proportion of enoximone treated patients withdrawn from the trial and the greater proportion admitted to hospital. The improvement seen in the disease-specific measure after 2 weeks (when deaths were 8 *v* 8, from table 3) was probably genuine, but the lack of differences at three months and one year was unlikely to be because of lack of power alone (although 95% confidence intervals for the differences in means were not quoted). Indeed, as one would have expected the group with more deaths to have a better average quality of life for the reasons given, the possibility arises that quality of life actually diminished on enoximone treatment.

Apart from the baseline comparison, we are not able to interpret the Nottingham Health Profile (NHP) data at all. For example, the median physical mobility score in the enoximone group was 22 at one year, but there is nothing to compare this with. We are not told what the median baseline score was for the enoximone treated survivors: and the placebo treated patients no longer form an adequate control group (as they are no longer matched with the enoximone group). It would have been interesting to see the results on the other NHP dimensions.

There are ways round this problem, but none is fully satisfactory. We can assign all patients who died to the bottom half of the distribution of quality of life scores (for example, by giving them all the worst possible score). The median is then not biased for comparative purposes. However, if more than half the subjects die the median becomes uninterpretable (although the Mann-Whitney U test remains valid). Alternatively, end points can be dichotomised into those alive with improved quality of life on one hand and those who died plus those who are alive with worse quality of life on the other. These can be analysed as proportions, but with consequent loss of statistical power. Finally, changes from baseline can be quoted for survivors only. These can be interpreted as uncontrolled observations (a so-called "before and after" study). So long as the questionnaire has reasonable test-retest reliability, a beneficial treatment effect is the most likely explanation for any improvement seen, although a placebo effect cannot be excluded.

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1 Cowley AJ, Skene AM on behalf of the Enoximone Investigators. Treatment of severe heart failure: quantity or quality of life? A trial of enoximone. *Br Heart J* 1994; 72:226–30.

Responses of plasma concentrations of A type natriuretic peptide and B type natriuretic peptide to alacepril, an angiotensin-converting enzyme inhibitor, in patients with congestive heart failure

SIR,—Yoshimura and colleagues showed that the response of plasma brain natriuretic peptide (BNP) after the administration of the angiotensin-converting enzyme inhibitor, alacepril, occurred later and lasted longer than the response of plasma atrial natriuretic peptide (ANP), and that the changes in pulmonary capillary wedge pressure did not correlate with plasma BNP.[1] This lack of correlation may be the result of this difference in responses.

It may be relevant to recall that BNP has a longer half life than ANP, and that the fall in BNP is bi-exponential, with a slow phase of about 20·7 minutes, as estimated by Nakao's group.[2] My own estimate of the slow half life was 37 minutes.[3] In addition, there may also be a qualitative difference in the synthesis and release of BNP. In